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Appln. No. 10/591,722
Supplemental Preliminary Amendment
Attorney Docket: MOEG-P100

Amendments to the Specification:

Please amend the paragraph bridging pages 16 and 17 as follows:

B represents $R_{25}(R_{26})N$ -, where R_{25} and R_{26} may form a ring. Examples of a ring formed by binding R_{25} and R_{26} directly together with a nitrogen atom to which they are bound include a pyrrolidine ring, a piperidine ring, a hexamethyleneimine ring, and a heptamethyleneimine ring. Examples of a ring formed by binding R_{25} and R_{26} through a heteroatom together with a nitrogen atom to which they are bound include a morpholine ring and a piperazine ring. Examples of a ring formed by binding R_{25} and R_{26} through an aromatic ring together with a nitrogen atom to which they are bound include a tetrahydroisoquinoline ring and a [[tetrahydroindole ring]] dihydroindole ring.

Please amend the second full paragraph on page 18 as follows:

In addition, examples of a pharmacologically acceptable salt include trifluoroacetates, hydrochlorides, acetates, sulfates, nitrates, lactates, maleates, methanesulfonates, toluenesulfonates, tartrates, citrates, oxalates, malonates, succinates, fumarates, propionates, butyrates, [[glucuronic acid, terephthalic acid, and phosphoric acid]] glucuronates, terephthalates, and phosphates. Preferable examples thereof include hydrochlorides, maleates, tartrates, and citrates. Tartrates are more preferable.

Please amend the last full paragraph on page 20 as follows:

N-(4-dipropylamino-butyl)-4-[[[(1-methyl-1H-imidazo-2-ylmethyl)] [(1-methyl-1H-imidazol-2-ylmethyl) -(5-methyl-pyridin-2-ylmethyl)-amino]-methyl]-benzamide [Compound No. 20]

Appln. No. 10/591,722
Supplemental Preliminary Amendment
Attorney Docket: MOEG-P100

Please amend the last full paragraph on page 23 as follows:

N-(4-[[[(1H-imidazol-2-ylmethyl)-[(5,6,7,8-tetrahydrohydro-quinolin-8-yl)]]
(5,6,7,8-tetrahydro-quinolin-8-yl)-amino]-methyl]-benzyl)-N-methyl-N',N'-dipropyl-
butane-1,4-diamine [Compound No. 49]

Please amend paragraph No. [0027] on page 32 as follows:

The pharmacologically acceptable salt is a salt which may be formed by the amine compound represented by the above described formula (1), and may be any salt that is pharmacologically acceptable. For example, trifluoroacetates, hydrochlorides, acetates, sulfates, nitrates, lactates, maleates, methanesulfonates, toluenesulfonates, tartrates, citrates, oxalates, malonates, succinates, fumarates, propionates, butyrates, [[glucuronic acid, terephthalic acid, phosphoric acid]] glucuronates, terephthalates, phosphates and the like can be given. Hydrochlorides, maleates, tartrates, and citrates are preferable, and tartrates are more preferable.

Please amend Example 19-1 bridging pages 118 and 119 as follows:

Example 19-1: Synthesis of
6-cyano-imidazo[1,2-a]pyridine-2-carboxylic acid ethyl ester

In ethanol (30 ml), 2-amino-5-cyanopyridine (2.45 g) was dissolved. The solution was added with 3-bromo-2-oxo-propionic acid ethyl ester (3.90 g) and the whole was refluxed under heating for 7 hours. The concentrated residue was dissolved in a minimum amount of a 10% hydrogen chloride/methanol solution and the solution was adjusted to pH 8 with a saturated aqueous sodium hydrogen carbonate solution. The

Appln. No. 10/591,722
Supplemental Preliminary Amendment
Attorney Docket: MOEG-P100

precipitate was collected by filtration, thereby obtaining the subject compound (3.81 g) as a pale-yellow solid.

MS(FAB,Pos.):m/z=216[M+H]⁺

¹H-NMR(500MHz,CDCl₃):δ=1.33(3H,t,J=7.1Hz),4.33(2H,q,J=7.1Hz),

7.61(1H,dd,J=1.7,9.6Hz),[[7.81(1H, J=0.7)] 7.81

(1H,ddc,J=0.7,1.0,9.6Hz),8.61(1H,d,J=0.7Hz),9.36(1H,dd,J=1.0,1.7Hz).

Please amend Example 19-2 on page 119 as follows:

Example 19-2: Synthesis of

6-cyano-imidazo[1,2-a]pyridine-2-carboxylic acid-(4-dipropylamino-butyl)-amide

The compound (263 mg) obtained in Example 1-2 was dissolved in dichloromethane (4.0 ml) and a 15% trimethyl aluminum/hexane solution (1.08 ml) was dropped thereto. The whole was stirred at room temperature for 15 minutes. The solution was added with the compound (300 mg) obtained in Example 19-1 and stirred for additional 20 hours. The resultant was heated to 40°C and stirred for additional 7 hours, and then 1 mol/l hydrochloric acid was added to stop the reaction, followed by extraction with chloroform. The organic layer was washed with a saturated aqueous sodium hydrogen carbonate solution, water, and a saturated saline solution and dried with anhydrous sodium sulfate. The residue obtained by distilling the solvent off was purified through silica gel column chromatography (chloroform/methanol), thereby obtaining the subject compound (237 mg) as a yellow solid.

MS(FAB,Pos.):m/z=342[M+H]⁺

Appln. No. 10/591,722
Supplemental Preliminary Amendment
Attorney Docket: MOEG-P100

¹H-NMR(500MHz,CDCl₃):δ=0.87(6H,t,J=3.7Hz),1.43-1.73(8H,m),2.39-2.50(6H,m),3.50(2H,dd,J=6.3,6.8Hz),7.35(1H,dd,J=1.7,9.6Hz),7.51(1H,br),[[7.66(1H, J=0.7)] 7.66(1H,ddc,J=0.7, 1.0,9.6Hz),8.26(1H,d,J=0.5Hz),8.64(1H,dd,J=1.0,1.7Hz).

Please amend Example 19-3 on page 120 as follows:

Example 19-3: Synthesis of

6-aminomethyl-5,6,7,8-tetrahydro-imidazo[1,2-a]pyridine-2-carboxylic acid-(4-dipropylamino-butyl)-amide

An ethanol solution (20 ml) containing the compound (40.2 mg) obtained in Example 19-2 was added with an ethanol suspension of Raney nickel and a 1 mol/l sodium hydroxide aqueous solution (2.0 ml), and the whole was stirred at room temperature for 14 hours under a hydrogen atmosphere. The catalyst was removed by filtration through Celite. The residue obtained by distilling the solvent off under reduced pressure was dissolved in chloroform, washed with water and a saturated saline solution, and dried with anhydrous sodium sulfate. The solvent was distilled off, thereby obtaining the subject compound (40.1 mg) as a yellow oily substance.

MS(FAB,Pos.):m/z=350[M+H]⁺

¹H-NMR(500MHz,CDCl₃):δ=0.86(6H,t,J=7.5Hz),2.03-2.13(2H,br),2.34-2.38(4H,m),2.44(2H,t,J=7.2Hz),2.75-2.82(2H,m),2.85(2H,dd,J=6.2,12.4Hz),[[2.97(1H, J=3.5)] 2.97(1H,ddc,J=3.5, 5.5,16.9Hz),3.40(2H,dd,J=6.8,13.4Hz),3.67(1H,dd,J=10.3,12.2Hz),[[4.18(1H, J=1.1)] 4.18(H,ddc,J=1.1, 5.2,12.4Hz),7.06(1H,br),7.40(1H,s).

Appln. No. 10/591,722
Supplemental Preliminary Amendment
Attorney Docket: MOEG-P100

Please amend the Production example 20 (Paragraph [0066]) on page 122 as follows:

Production example 20: Synthesis of

N-(4-dipropylamino-butyl)-4-[[[(1-methyl-1H-imidazo-2-ylmethyl)] [[1-methyl-1H-imidazol-2-ylmethyl]-(5-methyl-pyridin-2-ylmethyl)-amino]-methyl}-benzamide
[Compound No. 20]

Please amend the paragraph bridging pages 125 and 126 as follows:

MS(FAB,Pos.):m/z=505[M+H]⁺

¹H-NMR(500MHz,CDCl₃):δ=0.83(6H,t,J=7.3Hz),[[2.41(4H,qt)] 1.41(4H,qt
J=2.4,6.4Hz),1.55(2H,quint.,J=7.1Hz),1.65(2H,quint.,J=7.3Hz),2.32(3H,s),2.35(4H,t,J=2.
4Hz),2.44(2H,t,J=7.1Hz),3.45(2H,dt,J=5.6,6.8Hz),3.49(3H,s),3.65(3H,s),3.69(2H,s),3.70(
2H,s),6.94(1H,brt,J=5.0Hz),6.77(1H,d,J=1.2Hz),6.90(1H,d,J=1.2Hz),7.24(1H,d,J=7.8Hz),
7.38(2H,d,J=8.3Hz),7.46(1H,dd,J=1.7,8.0Hz),7.69(2H,d,J=8.6Hz),8.37(1H,d,J=1.5Hz).

Please amend Example 23-1 on page 132 as follows:

Example 23-1: Synthesis of

4-(t-butoxycarbonylamino-methyl)-benzoic acid methyl ester

4-aminomethylbenzoic acid methyl ester hydrochloride was subjected to desalting, thereby obtaining a free compound (20.2 g). The free compound was dissolved in anhydrous chloroform (400 ml) and added with triethylamine (34.1 ml) and [[di-t-

Appln. No. 10/591,722
Supplemental Preliminary Amendment
Attorney Docket: MOEG-P100

butylcarbonate]] di-t-butylidicarbonate (32.0 g), and the whole was stirred overnight at room temperature under a nitrogen atmosphere. After completion of the reaction, the solvent was distilled off. The resultant was dissolved in chloroform and added with distilled water, and the whole was stirred for a while. The resultant was subjected to extraction with chloroform and washed with a saturated saline solution. The organic layer was dried with anhydrous sodium sulfate. The solvent was distilled off, thereby obtaining the subject compound (35.7 g) as a colorless crystal.

MS(FAB,Pos.):m/z=266[M+H]⁺

Please amend the first full paragraph of Example 27-2 on page 145 as follows:

Example 27-2: Synthesis of

1-(4-dipropylamino-butyl)-3-(4-[[[(1H-imidazol-2-ylmethyl)-(1-methyl-1H-[[imidazol-2-ylmethyl)-amine]]] imidazol-2-ylmethyl]-amino]-methyl}-phenyl)-1,3-dimethyl-urea
[Compound No. 27]

Please amend the first full paragraph on page 179 as follows:

The compound (760 mg) obtained in Example 39-2, p-bromobenzaldehyde (690 mg), tri-o-tolylphosphine (103 mg), and palladium acetate (39 mg) were suspended in xylene (15 ml) and triethylamine (15 ml) and the whole was stirred at 130°C for 63 hours. The reaction solution was cooled to room temperature and then [[the solvent was]] concentrated under reduced pressure. The resultant residue was added with distilled water and the whole was subjected to extraction with dichloromethane. The organic layer was dried with anhydrous magnesium sulfate. The drying agent was filtrated out and the

Appln. No. 10/591,722
Supplemental Preliminary Amendment
Attorney Docket: MOEG-P100

organic layer was then concentrated under reduced pressure. The residue was purified through silica gel column chromatography (hexane/dichloromethane), thereby obtaining a yellow-white solid (0.91 g).

Please amend the paragraph bridging pages 179 and 180 as follows:

The compound (650 mg) obtained in Example 39-3 was dissolved in 1,2-dichloroethane (40 ml). The reaction solution was added with n-dipropylamine (0.29 ml) and sodium triacetoxymethylborohydride (600 mg) and the whole was stirred at room temperature for 18 hours. After that, n-dipropylamine (0.29 ml) was added thereto and the whole was stirred at 50°C for 1 hour. Then, sodium triacetoxymethylborohydride (600 mg) was added thereto and the whole was stirred at 50°C for 20 hours. [[After the reaction solution was cooled to room temperature, the solvent was concentrated under reduced pressure]] The reaction solution was cooled to room temperature and then concentrated under reduced pressure. The resultant residue was added with a 1 mol/l sodium hydroxide aqueous solution and the whole was subjected to extraction with chloroform. The organic layer was dried with anhydrous magnesium sulfate. The drying agent was filtrated out and the organic layer was then concentrated under reduced pressure. The residue was purified through silica gel column chromatography (chloroform/ethyl acetate), thereby obtaining the subject compound (646 mg) as a white solid.

Please amend the second full paragraph on page 182 as follows:

The compound (0.76 g) obtained in Example 39-3, p-bromobenzaldehyde (0.69 g), tri-o-tolylphosphine (103 mg), and palladium acetate (39 mg) were suspended in xylene

Appln. No. 10/591,722
Supplemental Preliminary Amendment
Attorney Docket: MOEG-P100

(15 ml) and triethylamine (15 ml) and the whole was stirred at 130°C for 63 hours. The reaction solution was cooled to room temperature and then [[the solvent was]] concentrated under reduced pressure. The resultant residue was added with distilled water and the whole was subjected to extraction with dichloromethane. The organic layer was dried with anhydrous magnesium sulfate. The drying agent was filtrated out and the organic layer was then concentrated under reduced pressure. The resultant residue was purified through silica gel column chromatography (hexane/dichloromethane), thereby obtaining the subject compound (25 mg) as a colorless oily substance.

Please amend the first full paragraph on page 183 as follows:

The compound (25 mg) obtained in Example 40-1 was dissolved in 1,2-dichloroethane (3.0 ml). The reaction solution was added with n-dipropylamine (0.019 ml) and sodium triacetoxymborohydride (36 mg) and the whole was stirred at room temperature for 62 hours. After that, n-dipropylamine (0.019 ml) and sodium triacetoxymborohydride (36 mg) were added thereto and the whole was stirred at 50°C for 3 hours. Then, n-dipropylamine (0.019 ml) and sodium triacetoxymborohydride (36 mg) were added thereto and the whole was refluxed under heating for 3 hours. [[After the reaction solution was cooled to room temperature, the solvent was concentrated under reduced pressure]] The reaction solution was cooled to room temperature and then concentrated under reduced pressure. The resultant residue was added with a 1 mol/l sodium hydroxide aqueous solution and the whole was subjected to extraction with chloroform. The organic layer was dried with anhydrous magnesium sulfate. The drying agent was filtrated out and the organic layer was then concentrated under reduced pressure. The resultant residue was purified through silica gel column chromatography

Appln. No. 10/591,722
Supplemental Preliminary Amendment
Attorney Docket: MOEG-P100

(chloroform/ethyl acetate), thereby obtaining the subject compound (27.0 mg) as a colorless oily substance.

$^1\text{H-NMR}$ (500MHz, CDCl_3): δ =0.86(6H,t,J=7.3Hz), 1.44-1.50(4H,m), 2.36-2.39(4H,m), 3.55(2H,s), 4.86(2H,s), 5.37(1H,d,J=1.2Hz), 5.44(1H,d,J=1.2Hz), 7.22-7.47(6H,m), 7.70-7.74(2H,m), 7.84-7.87(2H,m).

Please amend the first full paragraph on page 184 as follows:

The compound (110 mg) obtained in Example 40-2 was dissolved in methanol (6.0 ml). The reaction solution was added with hydrazine monohydrate (0.5 ml) and refluxed under heating for 1 hour. The reaction solution was cooled to room temperature and then [[the solvent was]] concentrated under reduced pressure. The resultant residue was added with distilled water and the whole was subjected to extraction with chloroform. The organic layer was dried with anhydrous magnesium sulfate. The drying agent was filtrated out and the organic layer was then concentrated under reduced pressure.

Please amend the first full paragraph on page 186 as follows:

The resultant was dissolved in 1,4-dioxane (10 ml). The reaction solution was added with 1 mol/l hydrochloric acid (3.0 ml) and the whole was refluxed under heating for 2 hours. The reaction solution was cooled to room temperature and [[the solvent was]] then concentrated under reduced pressure. A 1 mol/l sodium hydroxide aqueous solution was added thereto and the whole was subjected to extraction with chloroform. After that, the organic layer was washed with a saturated saline solution and the organic

Appln. No. 10/591,722
Supplemental Preliminary Amendment
Attorney Docket: MOEG-P100

layer was dried with anhydrous magnesium sulfate. The drying agent was filtrated out and the organic layer was then concentrated under reduced pressure.

Please amend the last full paragraph of Example 41-2 on page 187 as follows:

The reaction solution was added with hydrazine monohydrate (0.5 ml) and refluxed under heating for 2 hours. The reaction solution was cooled to room temperature and then [[the solvent was]] concentrated under reduced pressure. The resultant residue was added with distilled water and the whole was subjected to extraction with chloroform. The organic layer was dried with anhydrous magnesium sulfate. The drying agent was filtrated out and the organic layer was then concentrated under reduced pressure.

Please amend the second full paragraph on page 189 as follows:

The reaction solution was added with hydrazine monohydrate (0.5 ml) and refluxed under heating for 2 hours. The reaction solution was cooled to room temperature and then [[the solvent was]] concentrated under reduced pressure. The resultant was added with distilled water and the whole was subjected to extraction with chloroform. The organic layer was dried with anhydrous magnesium sulfate. The drying agent was filtrated out and the organic layer was then concentrated under reduced pressure.

Please amend Example 49 and Example 49-1 on page 220 as follows:

[Example 49]

Appln. No. 10/591,722
Supplemental Preliminary Amendment
Attorney Docket: MOEG-P100

[0114]

Production example 49: Synthesis of

N-(4- {[(1H-imidazol-2-ylmethyl)-[(5,6,7,8-tetrahydrohydro-quinolin-8-yl)]] (5,6,7,8-tetrahydro-quinolin-8-yl)-amino]-methyl}-benzyl)-N-methyl-N',N'-dipropyl-butane-1,4-diamine [Compound No. 49]

Example 49-1: Synthesis of

N-(4- {[(1H-imidazol-2-ylmethyl)-[(5,6,7,8-tetrahydrohydro-quinolin-8-yl)]] (5,6,7,8-tetrahydro-quinolin-8-yl)-amino]-methyl}-benzyl)-N-methyl-N',N'-dipropyl-butane-1,4-diamine [Compound No. 49]

Please amend the last paragraph on page 227 as follows:

[[The residue was dissolved in chloroform and the aqueous layer was extracted with chloroform.]] The residue was admixed with a 1 mol/l sodium hydroxide aqueous solution and the whole mixture was subjected to extraction with chloroform. The organic layer was washed with a saturated saline solution and dried with anhydrous sodium sulfate. The solvent was distilled off. The residue was purified through silica gel column chromatography (chloroform/methanol), thereby obtaining the subject compound (306 mg) as a pale-yellow oily substance.

MS(FAB,Pos.):m/z=465[M+H]⁺

Please amend the last full paragraph on page 229 as follows:

MS(FAB,Pos.):m/z=494[M+H]⁺

¹H-NMR(500MHz,[[CDCl₃]]) DMSO-d₆: δ=0.85

Appln. No. 10/591,722
Supplemental Preliminary Amendment
Attorney Docket: MOEG-P100

(6H,t,J=7.2Hz), 1.23-1.56(6H,m), 2.29-2.37(6H,m), 3.14(2H,t,J=7.0Hz),
3.23(2H,t,J=7.3Hz), 3.46(2H,s), 3.49(2H,s), 3.57(2H,s), 3.59(2H,s), 3.60(3H,s), 3.67(2H,s), 3.
68(2H,s), 4.38(2H,s), 4.53(2H,s), 6.88(1H,d,J=1.2Hz), 6.89(1H,d,J=1.4Hz), 7.00(1H,d,J=1.2
Hz), 7.01(2H,d,J=1.2Hz), 7.08(1H,s), 7.13(1H,s), 7.18(1H,d,J=8.3Hz), 7.22(1H,d,J=8.0Hz), 7
.37(1H,d,J=8.0Hz), 7.43(1H,d,J=8.3Hz), 8.20(1H,s), 8.28(1H,s), 12.38(1H,brs).

Please amend Example 54-2 on page 230 as follows:

Example 54-2: Synthesis of [(4-{{(1-carboxymethyl-1H-imidazol-2-ylmethyl)-(1-methyl-
1H-imidazol-2-ylmethyl)-amino}-methyl}-benzyl)-(4-dipropylamino-butyl)amino]-acetic
acid [Compound No. 54]

Please amend the first full paragraph on page 238 as follows:

[Example 59]

[0124]

Production example 59: Synthesis of [[2,2-dimethyl-propionic acid-1-[3-[(4-
dipropylamino-butyl)-(4-[(1H-imidazol-2-ylmethyl)-(1-methyl-1H-imidazol-2-ylmethyl)-
amino]-methyl)-benzyl]-amino]-propionyloxy methyl ester]] 2,2-dimethyl-propionic
acid-3-[(4-dipropylamino-butyl)-4-[(1H-imidazol-2-ylmethyl)-(1-methyl-1H-imidazol-
2-ylmethyl)-amino]-methyl]-benzyl]-amino]-propionyloxy methyl ester [Compound No.
65]

Example 59-1: Synthesis of [[2,2-dimethyl-propionic acid-1-[3-[(4-dipropylamino-butyl)-
(4-[(1H-imidazol-2-ylmethyl)-(1-methyl-1H-imidazol-2-ylmethyl)-amino]-methyl)-
benzyl]-amino]-propionyloxy methyl ester]] 2,2-dimethyl-propionic acid-3-[(4-

Appln. No. 10/591,722
Supplemental Preliminary Amendment
Attorney Docket: MOEG-P100

dipropylamino-butyl)-4-([(1H-imidazol-2-ylmethyl)-(1-methyl-1H-imidazol-2-ylmethyl)-
amino]-methyl]-benzyl]-amino]-propionyloxy methyl ester [Compound No. 65]

Please amend the last full paragraph on page 254 as follows:

MS(FAB,Pos.):m/z=668[M+H]⁺

¹H-NMR(500MHz,CDCl₃):δ=0.85(6H,t,J=7.3Hz),1.29(6H,dd,J=2.9, 6.1Hz),1.40-
1.44(8H,m),1.48(3H,d,J=5.4Hz),2.32-2.35(6H,m), 2.42(2H,t,J=6.8Hz),
2.48(2H,t,J=7.6Hz),2.79(2H,t,J=7.1Hz),3.46(2H,s),3.55(5H,s),3.62(2H,s),3.67(2H,s),4.87
(1H,quint.,J=6.3Hz),6.74(1H,q,J=5.4Hz),6.87(1H,d,J=1.2Hz),6.99(1H,d,J=1.2Hz),7.10(2
H,d,J=20.7Hz),[[7.26(2J,d,J=8.1Hz)]] 7.26(2H,d,J=8.1Hz),7.33 (2H,d,J=8.1Hz),
7.47(1H,br).

Please amend the paragraph bridging pages 259 and 260 as follows:

The compound (185.8 mg) obtained in Example 65-1 was dissolved in a small amount of water. The solution was added with chloroform and a 1 mol/l sodium hydroxide aqueous solution, and the organic layer and an oily substance were collected, followed by drying with anhydrous magnesium sulfate. After filtration, the solvent was distilled off. An anhydrous DMF solution (2 ml) containing the resultant sodium salt (143.6 mg) and N-(2-hydroxyethyl)morpholine (38 mg) was added with HOBt (37 mg) and WSCI hydrochloride (63 mg) and the whole was stirred overnight. After the solvent was distilled off, the resultant was dissolved in chloroform and washed with a saturated aqueous sodium hydrogen carbonate solution. The aqueous layer was extracted with chloroform and dried with anhydrous magnesium sulfate. The reaction mixture obtained

Appln. No. 10/591,722
Supplemental Preliminary Amendment
Attorney Docket: MOEG-P100

by distilling the solvent off was purified through silica gel column chromatography (chloroform). The resultant was dissolved in dioxane and a salt was allowed to precipitate with a 4 mol/l hydrogen chloride/dioxane solution. After the solvent was distilled off, the solid substance was pulverized and dried under reduced pressure, thereby obtaining a hydrochloride (143.9 mg) of the subject compound as a white solid.

Please amend the first full paragraph on page 312 as follows:

MS(FAB,Pos.):m/z=552[M+H]⁺

¹H-NMR (500MHz, CDCl₃): δ=0.86(6H,t,J=7.3Hz), 1.31(3H,t,J=7.1Hz), 1.39-1.48(5H,m), 1.53-1.63(1H,m), 1.67-1.73(2H,m), 2.25(3H,s), 2.33-2.37(4H,m), 2.41(2H,t,J=7.3Hz), 3.30(1H,t,J=7.6Hz), 3.47(2H,s), 3.56(3H,s), 3.59-3.62(3H,m), 3.68(2H,s), 3.76-3.79(1H,m), 4.16-4.24(2H,m), 6.87(1H,s), 7.00(1H,s), [7.10(2H,bd,J)] 7.10(2H,d,J=21.7Hz), 7.29(2H,d,J=8.3Hz), 7.34(2H,d,J=8.3Hz).

Please replace Example 94-1 on page 313 with the following Example 94-1:

[[Example 94-1: Synthesis of

(2S)-dipropylamino-5-[(4-[[[(1H-imidazol-2-ylmethyl)-(1-methyl-1H-imidazol-2-ylmethyl)-amino]-methyl]-benzyl)-methyl-amino]-pentanoic acid ethyl ester [Compound No. 113]]]

Example 94-1: Synthesis of

(S)-2-(9H-fluorene-9-ylmethoxycarbonylamino)-5-[(4-[[1H-imidazol-2-ylmethyl)-(1-methyl-1H-imidazol-2-ylmethyl)-amino]-methyl]-benzyl)-methyl-amino]-pentanoic acid

Appln. No. 10/591,722
Supplemental Preliminary Amendment
Attorney Docket: MOEG-P100

ethyl ester

Please amend the NMR data after the first full paragraph on page 322 as follows:

MS(FAB,Pos.):m/z=552[M+H]⁺

¹H-NMR(500MHz,[[CDCl₃]]) DMSO-d₆:d=0.79(6H,t,J=7.1Hz), 1.18(3H,t,J=7.1Hz),1.24-1.40(6H,m),1.47-1.62(2H,m),2.31-2.37(4H,m),2.43-2.49(2H,m),2.51(3H,s), 3.22(1H,t,J=8.1Hz),3.34-3.42(2H,br),3.49-3.52(4H,m),3.50(3H,s),3.56(2H,s),4.00-4.10(2H,m),6.80(1H,d,J=1.22Hz),6.98-7.06(2H,br), 7.07(1H,d,J=1.2Hz), 7.22(2H,d,J=8.1Hz),7.33(2H,d,J=8.1Hz).